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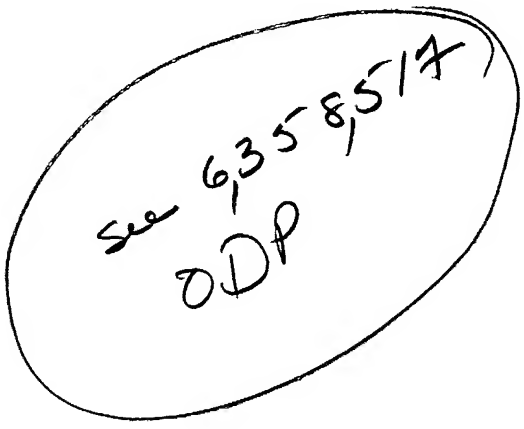

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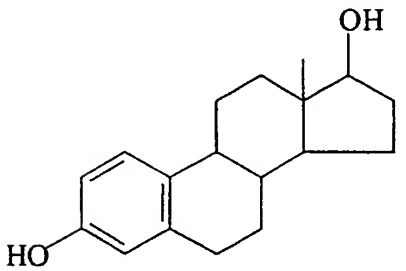
(54) Title: COSMETIC COMPOSITIONS CONTAINING RESVERATROL AND RETINOIDS

(57) Abstract: Cosmetic skin care compositions containing resveratrol in combination with selected retinoids are disclosed as well as methods of conditioning the skin by application of such compositions.

COSMETIC COMPOSITIONS CONTAINING RESVERATROL AND RETINOIDS

This invention relates to cosmetic compositions containing resveratrol in combination with retinoids and to methods of conditioning skin by the application of such compositions.

Estrogens and synthetic compounds which act like estrogens are known to increase the thickness of the dermal layer and reduce wrinkle formation in ageing skin. Changes in the skin such as skin dryness, loss of skin elasticity and plumpness occurring after menopause are attributed to the lack of estrogen production. Estrogen therapy prevents or slows down many of the changes associated with ageing skin (Creidi et al., Effect of a conjugated oestrogen cream (Premarin®) on ageing facial skin, Maturitas, 19, p.211-23, 1994). Natural estrogen, estradiol, has the following structure:



Retinol (vitamin A) is an endogenous compound which occurs naturally in the human body and is essential for normal epithelial cell differentiation. Natural and synthetic vitamin A derivatives have been used extensively in the treatment of a variety of skin disorders and as skin repair

and renewal agents. Retinoic acid has been used to treat a variety of skin conditions such as acne, wrinkles, psoriasis, age spots and skin discoloration.

Estradiol induces the expression of retinoid receptors in 2 different cell types. In mouse cervical epithelial cells estradiol stimulates the expression of retinoid X receptors and retinoic acid receptors (Exp Cell Res., 226: 273, 1996). In breast cancer cells estradiol induces the expression of a subtype of retinoic acid receptor gene expression (Mol. Endocrinol. 12: 882, 1998). Human skin expresses large amounts of the same types of retinoic acid receptors and retinoid X receptors (Voorhees *et al*, Skin Pharmacol., 6: 70, 1993). However, unlike the breast or cervix, skin is not a target organ for estrogen action.

Ptchelintsev *et al.* (US Patent 5,847,003 and US Patent 5,834,513) disclose compositions containing oxaacids and related compounds and which may further include numerous optional ingredients, among which are mentioned estradiol, retinoids and bioflavonoids.

The consumer demand for products containing plant extracts or ingredients derived from plants has been growing in recent years. Such products are perceived by consumers as pure and mild and superior to chemically synthesised products.

Phytoestrogens are natural compounds which have estrogen-like activity and which are found in plants. Some bioflavonoids, such as genistein and daidzein, are known phytoestrogens. WO 99/04747 (Unilever) teaches that

resveratrol, a compound found in a variety of plants, is a phytoestrogen and discloses cosmetic compositions containing resveratrol. One of the disclosed compositions also includes retinyl palmitate.

The present invention is based in part on the discovery that not all phytoestrogens and not all retinoids exhibit synergy when combined. The combination of resveratrol with selected retinoids, however, synergistically enhanced the beneficial effects of retinoids on skin.

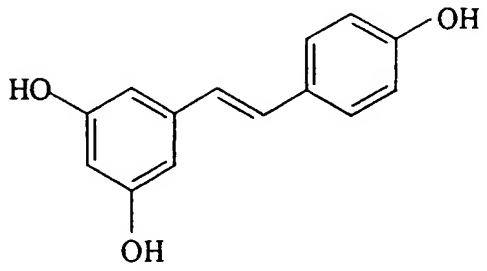
The art discussed above does not describe the presently claimed combinations of resveratrol and retinoids for skin care cosmetic use.

The present invention includes a cosmetic skin care composition comprising resveratrol in an amount of from 0.00001 to 10 wt.%, a retinoid selected from the group consisting of retinoic acid, retinol, retinyl acetate and retinyl linoleate, and a cosmetically acceptable vehicle.

The present invention also includes a method of improving or preventing the condition of wrinkled, lined, dry, flaky, aged or photo-damaged skin and of improving skin thickness, elasticity, flexibility, radiance, glow and plumpness, which method includes applying to the skin the inventive composition. Compositions of the invention are intended for topical application to mammalian skin which is already dry, flaky, lined, wrinkled, aged, photo-damaged, or the inventive compositions may be applied prophylactically to reduce the deteriorative changes.

Except in the examples, or where otherwise explicitly indicated, all numbers in this description indicating amounts of material or conditions of reaction, physical properties of materials and/or use are to be understood as modified by the word "about." All amounts are by weight of the composition, unless otherwise specified.

Resveratrol (also known as 5-parahydroxystyryl resorcinol, or 3,4',5-stilbenetriol) is an essential ingredient of the inventive composition. Resveratrol has the following structure:



Pure resveratrol may be obtained commercially from Sigma, and in crude form from other cosmetic suppliers such as DNP International, Pharma Science or Madis Botanicals.

In general, the amount of resveratrol in the inventive compositions is in the range of from 0.00001 to 10 % by weight composition. Preferably, in order to lower cost and maximise the effect, the amount of resveratrol is in the range of from 0.001% to 5% and most preferably is in the range of from 0.1% to 5%.

The inventive compositions further comprise a retinoid selected from the group consisting of retinoic acid, retinol, retinyl acetate, and retinyl linoleate. It has been found that these retinoids, but not retinyl palmitate, act synergistically in combination with resveratrol.

Preferably, the retinoid is selected from retinol, retinyl acetate and retinyl linoleate, because of its proven cosmetic efficacy.

The retinoid is generally employed in the inventive compositions in an amount of from 0.001 to 10%, preferably from 0.01 to 1%, most preferably from 0.01 to 0.5% by weight of the composition.

The composition according to the invention also comprises a cosmetically acceptable vehicle to act as a diluant, dispersant or carrier for resveratrol and the reinoid in the composition, so as to facilitate their distribution when the composition is applied to the skin.

Vehicles other than, or in addition to, water can include liquid or solid emollients, solvents, humectants, thickeners and powders. An especially preferred nonaqueous carrier is a polydimethyl siloxane and/or a polydimethyl phenyl siloxane. Suitable silicones of this invention may be those with viscosities ranging anywhere from about 10 to 10,000,000mm^2/s(centistokes) at 25°C. Especially desirable are mixtures of low and high viscosity silicones. These silicones are available from the General Electric

Company under trademarks Vicasil, SE and SF and from the Dow Corning Company under the 200 and 550 Series. The amounts of silicone which can be utilised in the compositions of the present invention range from 5% to 95%, preferably from 25% to 90% by weight of the composition.

The cosmetically acceptable vehicle will usually form from 5% to 99.9%, preferably from 25% to 80% by weight of the composition, and can, in the absence of other cosmetic adjuncts, form the balance of the composition. Conveniently, the vehicle is at least 80 wt.% water, by weight of the vehicle. Preferably, water comprises at least 50 wt.% of the inventive composition, most preferably from 60 to 80 wt.%, by weight of the composition.

As an optional skin benefit material or cosmetic adjunct, an oil or oily material may be present, together with an emulsifier to provide either a water-in-oil emulsion or an oil-in-water emulsion, depending largely on the average hydrophilic-lipophilic balance (HLB) of the emulsifier employed.

The inventive compositions preferably include sunscreens. Sunscreens include those materials commonly employed to block ultraviolet light. Illustrative compounds are the derivatives of PABA, cinnamate and salicylate. For example, octyl methoxycinnamate and 2-hydroxy-4-methoxy benzophenone (also known as oxybenzone) can be used. Octyl methoxycinnamate and 2-hydroxy-4-methoxy benzophenone are commercially available under the trademarks, Parsol MCX and Benzophenone-3, respectively. The exact amount of sunscreen

employed in the emulsions can vary depending upon the degree of protection desired from the sun's UV radiation.

Emollients are often incorporated into cosmetic compositions of the present invention. Levels of such emollients may range from 0.5% to 50%, preferably between 5% and 30% by weight of the total composition. Emollients may be classified under such general chemical categories as esters, fatty acids and alcohols, polyols and hydrocarbons.

Esters may be mono- or di-esters. Acceptable examples of fatty di-esters include dibutyl adipate, diethyl sebacate, diisopropyl dimerate, and dioctyl succinate. Acceptable branched chain fatty esters include 2-ethyl-hexyl myristate, isopropyl stearate and isostearyl palmitate. Acceptable tribasic acid esters include triisopropyl trilinoleate and trilauryl citrate. Acceptable straight chain fatty esters include lauryl palmitate, myristyl lactate, and stearyl oleate. Preferred esters include coco-caprylate/caprate (a blend of coco-caprylate and coco-caprate), propylene glycol myristyl ether acetate, diisopropyl adipate and cetyl octanoate.

Suitable fatty alcohols and acids include those compounds having from 10 to 20 carbon atoms. Especially preferred are such compounds such as cetyl, myristyl, palmitic and stearyl alcohols and acids.

Among the polyols which may serve as emollients are linear and branched chain alkyl polyhydroxyl compounds. For example, propylene glycol, sorbitol and glycerin are

preferred. Also useful may be polymeric polyols such as poly-propylene glycol and polyethylene glycol. Butylene and propylene glycol are also especially preferred as penetration enhancers.

Exemplary hydrocarbons which may serve as emollients are those having hydrocarbon chains anywhere from 12 to 30 carbon atoms. Specific examples include mineral oil, petroleum jelly, squalene and isoparaffins.

Another category of functional ingredients within the cosmetic compositions of the present invention are thickeners. A thickener will usually be present in amounts anywhere from 0.1 to 20% by weight, preferably from about 0.5% to 10% by weight of the composition. Exemplary thickeners are cross-linked polyacrylate materials available under the trademark Carbopol from the B.F. Goodrich Company. Gums may be employed such as xanthan, carrageenan, gelatin, karaya, pectin and locust beans gum. Under certain circumstances the thickening function may be accomplished by a material also serving as a silicone or emollient. For instance, silicone gums in excess of 10 centistokes and esters such as glycerol stearate have dual functionality.

Powders may be incorporated into the cosmetic composition of the invention. These powders include chalk, talc, kaolin, starch, smectite clays, chemically modified magnesium aluminum silicate, organically modified montmorillonite clay, hydrated aluminum silicate, fumed silica, aluminum starch octenyl succinate and mixtures thereof.

Other adjunct minor components may also be incorporated into the cosmetic compositions. These ingredients may include colouring agents, opacifiers and perfumes. Amounts of these other adjunct minor components may range anywhere from 0.001% up to 20% by weight of the composition.

The composition according to the invention is intended primarily as a product for topical cosmetic application to human skin, especially as an agent for conditioning, moisturising and smoothening the skin, and preventing or reducing the appearance of lined, wrinkled or aged skin.

In use, a small quantity of the composition, for example from 1 to 100ml, is applied to exposed areas of the skin, from a suitable container or applicator and, if necessary, it is then spread over and/or rubbed into the skin using the hand or fingers or a suitable device.

The topical skin treatment composition of the invention can be formulated as a lotion, a cream or a gel. The composition can be packaged in a suitable container to suit its viscosity and intended use by the consumer. For example, a lotion or cream can be packaged in a bottle or a roll-ball applicator, or a propellant-driven aerosol device or a container fitted with a pump suitable for finger operation. When the composition is a cream, it can simply be stored in a non-deformable bottle or squeeze container, such as a tube or a lidded jar. The composition may also be included in capsules such as those described in U.S. Patent 5,063,507, incorporated by reference herein. The invention

accordingly also provides a closed container containing a cosmetically acceptable composition as herein defined.

The following specific examples further illustrate the invention, but the invention is not limited thereto. In all examples, resveratrol was obtained from Sigma. Retinoids were obtained from Sigma. The student "t-test" was used to calculate all the p-values.

The following methods were employed:

Cell culture method:
Human adult fibroblasts obtained from the sun-protected inner arm of a 25-30 year female volunteer were used. Cells were grown in 1:1 DMEM/Hams F12 media containing 10% FBS, maintained at 37°C in a 5% CO_2 atmosphere under normal atmospheric oxygen tension. Third passage adult fibroblasts were grown in DMEM media with 10% FBS in 12-well plates at a seeding density of 40,000 cells/ml/well. The cells at 80% confluence were rinsed in serum free and phenol red free (PRF) DMEM media twice. Cells were pre-treated with resveratrol for 4 hours and then dosed with retinoids and incubated for a further 48 hours. After the incubation, the wells were washed twice with 1X PBS and the cell monolayer was harvested in 100µl cell lysis buffer (contained 1X PBS, 1% Triton X, 0.5% sodium deoxycholate, 0.1% SDS containing protease inhibitor (10mg/ml PMSF in isopropanol, 10µl/ml). The suspension was spun at 14000rpm for 10 minutes, the supernatant collected and an aliquot of this supernatant was used for protein quantification. Protein concentration was determined using Pierce protein kit. The remainder of 100µl

supernatant (cell lysate) was denatured in a mixture of 40µl sample buffer (NOVEX) and 0.5% Beta mercaptoethanol (BME) and by boiling the sample for 5 minutes.

Pig skin organ culture method:
7mm pig skin biopsies were taken, plated in serum free DMEM, and incubated for 2 days. The media was then switched to phenol-red free media. The biopsies were topically treated with resveratrol for 24 hrs in 5 µl ethanol per biopsy. After 24 hours, retinoids were topically applied to the biopsies. The treated biopsies were incubated for 4 days thereafter. After the treatment phase, the biopsies were rinsed in 1X phosphate-buffer twice and then frozen at -20°C for future use. The epidermis and dermis was separated by freezing and scraping off the epidermis. The epidermis was collected and homogenised in lysis buffer (contains 1X PBS, 1% Triton X, 0.5% sodium deoxycholate, 0.1% SDS containing protease inhibitor (10mg/ml PMSF in isopropanol at 10µl/ml, Aprotinin 30µl/ml and 100mM sodium orthovanadate at 10µl/ml). This homogenate was then spun at 14000 rpm and the supernatant was collected for determining protein (aliquot of the supernatant for protein determination).

Detection of Cellular Retinoic Acid Binding Protein 2 (CRABP-2) in fibroblasts and pig skin biopsies:
Within the cells, retinol and retinoic acid are bound to specific cellular binding proteins. Two of the major proteins are CRABP-1 and CRABP-2 (Roos *et al.*, Pharmacological reviews: 50, 315-333, 1998). These proteins regulate the intracellular concentration of retinoids by acting as either storage or shuttle proteins in retinoid

metabolism. The levels of CRABP protein are regulated by the amount of retinoic acid within the cells. Higher cellular levels of retinoids increase the expression of CRABP-2. Therefore, the amount of this protein in the cells, is a measure of the retinoid activity of the cells. Skin cells contain high levels of CRABP-2 both in the epidermis and the dermis. The CRABP-2 response to retinoid administration in fibroblasts *in vitro* is used as a reproducible measure of retinoid bioactivity that predict human skin responses (Elder *et al.*, J. Invest. Dermatol., 106: 517-521, 1996). An increase in CRABP-2 is also associated with increased epidermal differentiation, and dermal retinoid action. Therefore, in these studies we used CRABP-2 expression of fibroblasts and pig skin epidermis as a measure of retinoid activity leading to increased epidermal differentiation (skin conditioning and dry skin benefit) and dermal collagen and extracellular matrix synthesis (antiageing, anti wrinkling benefits).

To measure the levels of CRABP-2 in the fibroblast and pig skin extracts prepared as described above, the cell supernatant was re-suspended in 4X sample buffer and 10% BME, boiled for 5 minutes and used for western blotting. Equal amounts of protein were loaded onto 16% Tris-glycine gels for CRABP-2 protein analysis by SDS-PAGE and Western Immuno-blotting. The gels were transferred to PVDF membranes and Western Blotting was carried out using monoclonal antibodies to CRABP-2 according to standard procedures. The CRABP-2 protein band was visualised in the Western Blots using the chemiluminescence system obtained from Boehringer Mannheim (Indianopolis, IN). The bands in the film were

quantified by densitometric scanning, the data from triplicate samples were calculated as % of control and expressed in the following tables as % increase over control (with control as 100%) +/- standard deviation.

EXAMPLE 1

The effect on skin of using the combination of resveratrol with retinol or retinoic acid was tested using pig skin organ culture method. The results that were obtained are summarised in Table 1.

The control in the first experiment was 0.0763+/-0.0259 and in the second experiment 0.11+/-1.01 OD.

TABLE 1

	Alone	p-value (vs. control)	Retinoid + resveratrol	p-value (vs. Retinoid)	Synergy at p<0.05
Experiment 1					
Control	100+/-33.9	----			
1 µM retinoic acid	3207+/-716	0.003			
50 µM Resveratrol	143+/-64	0.448	930+/-80	0.027	Yes
Experiment 2					
Control	100+/-9	----			
5 µM retinol	345+/-89	0.058			
20 µM Resveratrol	242+/-189	0.470	1581+/-81	0.003	Yes

It can be seen from the results in Table 1 that resveratrol alone showed only minimal, insignificant effects on CRABP-2

expression. Retinol and retinoic acid showed significantly higher stimulation of CRABP-2 expression. When the pig skin epidermis was pre-treated with resveratrol, resveratrol synergistically enhanced retinol and retinoic acid activity.

EXAMPLE 2

The effect on skin of using resveratrol with retinoids, including retinyl esters was investigated in human skin fibroblasts. The results that were obtained in 2 separate experiments are summarised in Tables 2A and 2B, respectively.

TABLE 2A

	CRAB-2 production	% of Control	p value vs. Control	P value vs. retiniods	p value vs. resveratrol	Synergy at p?
Control	1.546+/-0.44	100+/-28	1			
10nM Retinoic acid	2.566+/-0.19	165+/-12	0.02	1		
1nM Retinoic acid	2.056+/-0.50	132+/-32	0.25	1		
100nM Retinyl Linoieate	0.88+/-0.23	57+/-14	0.08	1		
100nM Retinyl Palmitate	0.376+/-0.11	25+/-7	0.01	1		
100nM Retinyl Acetate	0.876+/-0.20	56+/-13	0.07	1		
10µM Resveratrol	0.416+/-0.12	27+/-8	0.013		1	
10µM Resveratrol + 10nM Retinoic acid	4.926+/-0.29	318+/-19	0.00039	0.000318	1.70E-05	Yes
10µM Resveratrol + 1nM Retinoic acid	3.54+/-0.60	229+/-38	0.0098	0.03	0.000916	Yes
10µM Resveratrol + 100nM Retinyl linoleate	1.911+/-0.022	124+/-14	0.23	0.016	0.002253	Yes
10µM Resveratrol + 100nM Retinyl palmitate	0.576+/-0.25	37+/-16	0.03	0.288	0.3888	No
10µM Resveratrol + 100nM Retinyl acetate	0.75+/-0.28	49+/-18	0.05	0.56	0.1416	No

TABLE 2B

	CRABP-2 production	% as Control	p value vs. control	p value vs. retinoids	p Value vs. active	Synergy at p?
Control	0.57+/-0.18	100+/-31	1			
10µM Retinoic acid	3.27+/-0.34	574+/-60	0.000275	1		
1uM Retinol	1.54+/-0.41	270+/-73	0.0208	1		
1µM Retinyl Palmitate	2.87+/-1.48	503+/-260	0.062	1		
1µM Retinyl Linoleate	0.64+/-0.4.3	112+/-75	0.8	1		
1µM Retinyl Acetate	1.01+/-0.58	178+/-102	0.27	1		
10µM Resveratrol	0.185+/-0.007	32+/-1	0.06		1	
10µM Resveratrol + 10nM Retinoic acid	4.78+/-0.02	839+/-4	7.10E-05	0.0098	1.18E-05	Yes
10µM Resveratrol + 1uM Retinol	1.75+/-0.55	307+/-96	0.034	0.611	0.05	No
10µM Resveratrol + 1µM Retinyl Palmitate	0.51+/-0.4	90+/-71	0.845	0.067	0.35	No
10µM Resveratrol + 1µM Retinyl Linoleate	3.66+/-0.99	641+/-174	0.006	0.0085	0.01	Yes
10µM Resveratrol + 1µM Retinyl Acetate	3.78+/-0.77	664+/-135	0.002	0.0077	0.0082	Yes

It can be seen from the results in Tables 2A and 2B that resveratrol in combination with retinoids, synergistically stimulated CRABP-2 expression in skin fibroblasts, except when resveratrol was combined with retinyl palmitate (which was not effective in either of the experiments). Retinol was effective in the second experiment where it was tested (retinol was not tested in the first experiment -- Table 2A). Low levels of retinyl acetate (100nm) either alone or in combination with resveratrol, were ineffective. However, at higher levels (Table 2B) retinyl acetate stimulated CRABP-2 expression in the presence of resveratrol.

COMPARATIVE EXAMPLE 3

This example investigated the effect on skin of a combination of soy extract (which is a known phytoestrogen) and retinoids.

In this example, soy powder obtained from ADM (Nova Soy) was dissolved in ethanol as a 1 mg/ml solution, heated to 70°C for half hour and filtered. The alcoholic extract was used to test in the assays. The results that were obtained are summarised in Table 3.

TABLE 3

	CRABP-2 production	% as Control	p value vs Control	p value vs retinoids	Synergy at p?
Control	0.450+/-0.18	100+/-42	1		
10nM Retinoic acid	1.201+/-0.36	266+/-80	0.033	1	
100nM Retinol	1.387+/-0.49	308+/-108	0.036	1	
100nM Retinyl Linoleate	1.141+/-0.57	253+/-127	0.118	1	
100nM Retinyl Palmitate	1.143+/-0.45	254+/-101	0.072	1	
100nM Retinyl Acetate	0.561+/-0.19	124+/-42	0.51	1	
0.0001% Soy	1.808+/-0.746	401+/-165	0.047		
0.0001% Soy+10nM Retinoic acid	2.206+/-0.73	490+/-162		0.099	No
0.0001% Soy+100nM Retinol	1.553+/-0.98	345+/-218		0.805	No
0.0001% Soy+100nM Retinyl Linoleate	1.637+/-0.45	363+/-100		0.304	No
0.0001% Soy+100nM Retinyl Palmitate	1.143+/-0.24	254+/-55		0.123	No
0.0001% Soy+100nM Retinyl Acetate	0.782+/-0.38	173+/-84		0.419	No

As seen from Table 3, soy extract alone stimulated CRABP-2 expression of fibroblasts by 400% of control (to the same levels as retinoids). The different retinoids stimulated CRABP-2 expression from 200-400% of control. However, when combined together, soy did not synergize with the different retinoids. The combination was in most cases even less active than either agent alone. Thus, soy extract, although being a phytoestrogen, did not exhibit synergy with retinoids in the expression of CRABP-2 in fibroblasts.

Examples 4- 9 illustrate skin care compositions according to the present invention. The compositions can be processed in a conventional manner and are suitable for cosmetic use. In particular, the compositions are suitable for application to wrinkled, lined, rough, dry, flaky, aged and/or UV-damaged skin to improve the appearance and the feel thereof as well as for application to healthy skin to prevent or retard deterioration thereof.

EXAMPLE 4

This example illustrates a high internal phase water-in-oil emulsion incorporating the inventive composition.

	% w/w
Resveratrol	0.5
Retinol	0.5
1,3-dimethyl-2-imidazolidinone	0.2
Brij 92*	5
Bentone 38	0.5
$MgSO_4 7H_2O$	0.3
Butylated hydroxy toluene	0.01
Perfume	qs
Water	to 100

* Brij 92 is polyoxyethylene (2) oleyl ether

EXAMPLE 5

This example illustrates an oil-in-water cream incorporating the inventive composition.

	% w/w
Resveratrol	2
Retinyl linoleate	0.5
Glycolic Acid	8
Mineral oil	4
1,3-dimethyl-2-imidazolidinone	1
Brij 56*	4
Alfol 16RD*	4
Triethanolamine	0.75
Butane-1,3-diol	3
Xanthan gum	0.3
Perfume	qs
Butylated hydroxy toluene	0.01
Water	to 100

* Brij 56 is cetyl alcohol POE (10)
Alfol 16RD is cetyl alcohol

EXAMPLE 6

This example illustrates an alcoholic lotion incorporating the composition according to the invention.

	[redacted]
Resveratrol	5
Retinyl acetate	0.5
Retinyl Linoleate	1.0
1,3-dimethyl-2-imidazolidinone	0.1
Ethanol	40
Perfume	qs
Butylated hydroxy toluene	0.01
Water	to 100

EXAMPLE 7

This example illustrates another alcoholic lotion containing the inventive composition.

	w/w
Resveratrol	5
Retinol	1.0
1,3-dimethyl-2-imidazolidinone	0.01
Ethanol	40
Antioxidant	0.1
Perfume	qs
Water	to 100

EXAMPLE 8

This example illustrates a suncare cream incorporating the composition of the invention:

	w/w
Resveratrol	2
Retinyl Linoleate	2.0
1,3-dimethyl-2-imidazolidinone	0.2
Silicone oil 200 cts	7.5
Glycerylmonostearate	3
Cetosteryl alcohol	1.6
Polyoxyethylene-(20)-cetyl alcohol	1.4
Xanthan gum	0.5
Parsol 1789	1.5
Octyl methoxycinnate (PARSOL MCX)	7
Perfume	qs
Color	qs
Water	to 100

EXAMPLE 9

This example illustrates a non-aqueous skin care composition incorporating the inventive combination.

	% w/w
Resveratrol	5
Retinol	1.0
1,3-dimethyl-2-imidazolidinone	1
Retinyl Linoleate	1.0
Silicone gum SE-30[1]	10
Silicone fluid 345[2]	20
Silicone fluid 344[3]	to 100
Squalene	10
Linoleic acid	0.01
Cholesterol	0.03
2-hydroxy-n-octanoic acid	0.7
Vitamin E linoleate	0.5
Herbal oil	0.5
Ethanol	2

[1] A dimethyl silicone polymer having a molecular weight of at least 50,000 and a viscosity of at least 10,000 centistokes at 25°C, available from GEC

[2] Dimethyl siloxane cyclic pentamer, available from Dow Corning Corp.

[3] Dimethyl siloxane tetramer, available from Dow Corning Corp.

It should be understood that the specific forms of the invention herein illustrated and described are intended to be representative only. Changes, including but not limited to those suggested in this specification, may be made in the illustrated embodiments without departing from the clear teachings of the disclosure. Accordingly, reference should be made to the following appended claims in determining the full scope of the invention.

CLAIMS:

1. A cosmetic skin care composition comprising:

(i) resveratrol in an amount of from 0.00001 to 10 wt.%;

(ii) a retinoid selected from retinoic acid, retinol, retinyl acetate and retinyl linoleate; and

(iii) a cosmetically acceptable vehicle.

2. A cosmetic skin care composition according to claim 1, wherein the resveratrol is present at an amount of 0.0001 to 5% by weight of the composition.

3. A cosmetic composition according to claim 1 or claim 2, wherein the retinoid is present at a level of 0.001 to 10% by weight.

4. A cosmetic method of improving the appearance of wrinkled, lined, dry, flaky, aged or photodamaged skin and improving skin thickness, elasticity, flexibility and plumpness, the method comprising applying to the skin the composition of any of claims 1 to 3.

5. A cosmetic method of increasing the level of cellular retinoic acid binding protein in the skin, the method comprising applying to the skin the composition of any of claims 1 to 3.

INTERNATIONAL SEARCH REPORT

Interr. ıal Application No
PCT/EP 00/09515

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K7/48

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
WPI Data, PAJ, EPO-Internal, MEDLINE, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	FR 2 777 186 A (L'OREAL) 15 October 1999 (1999-10-15) claims 1-22 page 8, line 36	1-5
A	FR 2 777 183 A (L'OREAL) 15 October 1999 (1999-10-15) claims 1-8 page 8, line 14	1-5
A	WO 99 04747 A (UNILEVER PLC ET AL.) 4 February 1999 (1999-02-04) cited in the application claims 1-7 page 26, line 29	1-5

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"O" document referring to an oral disclosure, use, exhibition or other means

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Date of the actual completion of the international search	Date of mailing of the international search report
24 January 2001	31/01/2001

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INTERNATIONAL SEARCH REPORT

Information on patent family members

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